## REMARKS

Claims 70-129, 131-133, 135-137, and 139-141 have been rejected and remain pending. The title has been amended herein to indicate that the application relates to methods for treating and preventing asthma and non-invasive fungus-induced rhinosinusitis. No new matter is added by this amendment. In light of the following remarks, Applicant respectfully requests reconsideration and allowance of claims 70-129, 131-133, 135-137, and 139-141.

Withdrawn rejections

Applicant acknowledges withdrawal of the rejections under 35 U.S.C. §112, first paragraph.

Information Disclosure Statements

Applicant respectfully requests consideration of the references designated "AJ" and "AL" on sheet 1 of the PTO-1449 form submitted August 1, 2000. For the Examiner's convenience, a corrected PTO-1449 form is attached hereto as well as copies of the two references. This corrected PTO-1449 form provides a more complete citation of the two references.

Applicant also respectfully requests an initialed copy of the two PTO-1449 forms submitted April 23, 2001. For the Examiner's convenience, copies of the two PTO-1440 forms are attached hereto.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 70-129, 131-133, 135-137, and 139-141 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that the "phrase 'in an amount, at a frequency, and for a duration effective to eliminate said asthma and said non-invasive fungus-induced rhinosinusitis' is indefinite in the context employed because (i) it is relative; and (ii) the phrase is neither specified in the specification, nor would it be apparent to one of ordinary skill in the art."

Applicant respectfully disagrees. The phrase "in an amount, at a frequency, and for a duration effective to reduce or eliminate said asthma and said non-invasive fungus-induced

rhinosinusitis" is not indefinite. Present claim 70 recites mucoadministering a formulation in an amount, at a frequency, and for a duration effective to reduce or eliminate asthma and non-invasive fungus-induced rhinosinusitis. A person having ordinary skill in the art reading Applicant's specification would have understood that the terms "in an amount," "at a frequency," and "for a duration" are adequately described in Applicant's specification and have a clear and unambiguous meaning. For example, the section at page 40, lines 1-12 of Applicant's specification describes the meaning of an effective amount as follows:

> An effective amount of an antifungal agent or formulation containing an antifungal agent can be any amount that reduces, prevents, or eliminates non-invasive fungus-induced mucositis upon mucoadministration in a mammal without producing significant toxicity to the mammal. Typically, an effective amount can be any amount greater than or equal to the minimum inhibitory concentration (MIC) for a fungal organism or isolate present within a particular individual's mucus that does not induce significant toxicity to the individual upon mucoadministration. Some antifungal agents may have a relatively large concentration range that is effective while others may have a relatively narrow effective concentration range. In addition, the effective amount can vary depending upon the specific fungal organism or isolate since certain organisms and isolates are more or less susceptible to particular antifungal agents.

In addition, the section at page 42, lines 4-8 of Applicant's specification describes the meaning of an effective frequency as follows:

> The frequency of mucoadministration can be any frequency that reduces, prevents, or eliminates non-invasive fungus-induced mucositis in a mammal without producing significant toxicity to the mammal. For example, the frequency of mucoadministration can be from about four times a day to about once a month, or more specifically, from about twice a day to about once a week.

Further, the section at page 42, lines 16-25 of Applicant's specification describes the meaning of effective durations as follows:

> An effective duration for antifungal agent mucoadministration can be any duration that reduces, prevents, or eliminates non-invasive fungus-induced mucositis in a mammal without producing significant toxicity to the mammal. Thus, the effective duration can vary from several days to several weeks, months, or years. In general, the effective duration for the treatment of non-invasive fungus-induced mucositis can range in duration from several days to several months. Once the antifungal applications are stopped, however, non-invasive fungus-induced mucositis may return. Thus, the effective duration for the

> prevention of non-invasive fungus-induced mucositis can last in some cases for as long as the individual is alive.

Given the description provided throughout Applicant's specification, a person having ordinary skill in the art would have clearly understood the presently claimed invention. Moreover, a person having ordinary skill in the art reading Applicant's specification would have understood that the present claims require mucoadministering a formulation in an amount, at a frequency, and for a duration effective to achieve a clinically measurable endpoint (e.g., the reduction or elimination of asthma and non-invasive fungus-induced rhinosinusitis).

With respect to the Examiner's assertion that the phrase is not specified in the specification, Applicant respectfully submits that Applicant's specification discloses substantial information about effective amounts, effective frequencies, and effective durations. In fact, Examples 2 and 5 disclose the treatment of 28 asthma patients who also are non-invasive fungus-induced rhinosinusitis patients. Specifically, the section at page 66, lines 16-26 of Applicant's specification discloses the treatment of 28 patients having both asthma and non-invasive fungus-induced rhinosinusitis as follows:

> Thirty-seven of the 53 patients in the study described in Example 2 had previously diagnosed chronic asthma. After three months of antifungal treatment, 28 of the 37 asthmatic patients upon questioning declared an improvement or complete elimination of asthma symptoms. Four of these 28 were analyzed using a pulmonary function test after antifungal treatment since they had taken a similar test before antifungal treatment. Comparing the results before and after antifungal treatment confirmed that all four of these asthma patients had improved pulmonary function. In addition, 26 of the 28 patients no longer exhibiting asthma symptoms stopped taking their asthma medication. Twenty-three of these 26 patients were taking systemic steroids for asthma prior to the antifungal treatment, but none have subsequently taken steroids after starting the antifungal treatment.

Example 2 of Applicant's specification discloses an amount, frequency, and duration effective to treat patients having both asthma and non-invasive fungus-induced rhinosinusitis. Specifically, the section from page 58, line 24 through page 59, line 1 of Applicant's specification discloses the following:

> The 125 non-invasive fungus-induced rhinosinusitis patients were started on an antifungal treatment of about 20 mL of an amphotericin B solution per nostril,

> two to four times daily for at least three months. The concentration of the amphotericin B solution was about 100 mg per liter of saline or water. A 20 mL bulb was used by the patient to mucoadminister the amphotericin B solution into the patient's nasal-paranasal anatomy.

Thus, a person of ordinary skill in the art reading Applicant's specification including the working examples disclosing treatment of 28 patients would have appreciated that Applicant's specification specifies effective amounts, effective frequencies, and effective durations in the context of the claimed subject matter.

Taken together, a person of ordinary skill in the art reading the present claims in light of Applicant's specification would have understood the metes and bounds of the presently claimed invention. In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 70-129, 131-133, 135-137, and 139-141 under 35 U.S.C. §112, second paragraph.

Comment regarding 37 C.F.R. §1.78(b)

The Examiner stated that the claims of this application conflict with claims of Application Nos. 09/177,273; 09/177,164; 09/177,165; 09/176,990; and 09/177,659.

Applicant respectfully submits that Applicant's different applications do not contain conflicting claims. The present application is directed to reducing or eliminating asthma and non-invasive fungus-induced rhinosinusitis. The 09/177,273 application is a recently allowed application directed to reducing or eliminating non-invasive fungus-induced intestinal mucositis. The 09/177,164 application is directed to reducing or eliminating non-invasive fungus-induced rhinosinusitis. The 09/176,990 application issued as U.S. Patent No. 6,207,703 reciting methods for reducing or eliminating symptoms of asthma. The 09/177,659 application is directed to reducing or eliminating non-invasive fungus-induced otitis media. It is noted that the 09/177,165 application cited by the Examiner appears to have been included in error. Applicant is unfamiliar with the 09/177,165 application.

In light of the above, Applicant respectfully requests allowance of claims 70-129, 131-133, 135-137, and 139-141.

## CONCLUSION

Applicant submits that claims 70-129, 131-133, 135-137, and 139-141 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. The Assistant Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

Date: June 6, 2001

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**Version with markings to show changes made**

In the specification:

The Title beginning at page 1, line 2 has been amended as follows:

METHODS [AND MATERIALS] FOR TREATING AND PREVENTING [INFLAMMATION OF MUCOSAL TISSUE] ASTHMA AND NON-INVASIVE FUNGUS-INDUCED RHINOSINUSITIS